REMARKS

Applicants note that the IDS previously filed in this case was apparently not matched up with the case. Applicants are submitting herewith a copy of the IDS as filed and documentation of the filing.

Claims 1-20 are pending in the application. Claims 1, 3, 8, 9, 10, 12, 13, 17, 18, 19, and 20 have been amended. New claims 21-33 have been added. Support for the amendments and newly added claims can be found in the original claims as well as in the specification. Newly added claims 21-28 emphasize the importance to the invention that the secondary nucleotide sequences of the claims share a high percentage of identity to the exemplary nucleotide sequences set forth in SEQ ID NOs: 2, 4, 7, or 10. Newly added claim 29 emphasizes the importance to the invention that the promoters of the claims may be either the same promoter or different promoters. Newly added claims 30-33 emphasize the importance to the invention that the primary nucleotide sequence of the claims encodes a polypeptide having fumonisin esterase activity or amine oxidase activity.

The newly submitted sequence listing includes newly added sequences 12-33. These sequences were incorporated into the present specification by reference as detailed in the amendments to the specification above and thus the addition of these sequences to the sequence listing does not constitute new matter.

No new matter has been added by way of amendment. Reexamination and reconsideration of the claims are respectfully requested.

The Invention

The invention relates to compositions and methods for detoxification or degradation of fumonisin or AP1. The enzymes and nucleotide sequences of the present invention provide a means for continued catabolism of the fumonisin-degradation products obtained by degradation with other enzymes, such as, for example, previously-described carboxylesterase and amine oxidase enzymes.

The Rejection of Claims Under 35 U.S.C.§112, Second Paragraph, Should Be Withdrawn

The Office Action (8/27/02, page 2, #2) has rejected claims 1-20 as being indefinite for various reasons. Claims 1, 8, 9, 10, 13, 17, 18, 19, and 20 have been amended in accordance with the specific suggestions provided in the Office Action. New claims 21-33 have been drafted taking into consideration the comments in the Office Action.

The Office Action has rejected claims 2, 3, 11, and 12 as indefinite for their reference to "ESP1," BEST1," and "APAO," which are described in the Office Action as not being defined in the specification. Applicants believe that these terms are sufficiently defined in the specification. Particularly, page 11 of the specification states that ESP1 and BEST1 are described in specific U.S. patents and applications. Because these specified applications have issued, the specification has been updated to include the corresponding U.S. patent numbers. These referenced patents (and applications) are incorporated by reference into the present specification, as indicated on page 49.

ESP1 is described in U.S. Patent No. 5,716,820 (column 25, lines 9 *et seq.*), *inter alia*, as a "full length, 1937 bp cDNA clone from *Exophiala spinifera* 2141.10 (abbreviated ESP1) [that] contains an open reading frame of 537 amino acids as shown below (SEQUENCE I.D. NO. 10)." The nucleotide sequence of ESP1 is included in the substitute sequence listing submitted herewith as SEQ ID NO:12. BEST1 is described in U.S. Patent No. 6,025,188 (column 3), *inter alia*, as the fumonisin-degrading enzyme for the bacterium of ATCC 55552 and is further described in lines 35 *et seq.* of column 25 as "a protein (called BEST1, SEQ ID NO:12) ...giving a mature protein with a calculated molecular weight of 51,495.63 daltons and a pI of 8.19." The nucleotide sequence of BEST1 is set forth in SEQ ID NO:11 of U.S. Pat. No. 6,025,188 and is included with the substitute sequence listing submitted herewith as SEQ ID NO:14. The amino acid sequence of the BEST1 polypeptide is set forth in SEQ ID NO:15 of the substitute sequence listing submitted herewith.

As indicated on page 9 of the specification, APAO (amino polyolamine oxidase) enzymes are described in U.S. Pat. Nos. 6,211,434 and 6,211,435, and these APAO sequences have been incorporated into the substitute sequence listing submitted herewith. Other amine oxidase enzymes are known in the art. See, for example, U.S. Pat. No. 5,792,931, issued August 11, 1998. Claims 3 and 12 have been amended to include the term "amino polyolamine oxidase" rather than APAO, as recommended by the Examiner. However, the terms "ESP1" and "BEST1" are not acronyms of a type of enzyme but rather are the specific names of particular cloned enzymes, as described in the specification, and thus Applicants submit that these terms are both clear and specific.

In view of the above remarks and amendments, Applicants respectfully submit that the rejection of claims under 35 U.S.C. §112, second paragraph, should be withdrawn and not applied to the newly added claims.

The Rejection of Claims Under 35 U.S.C.§112, First Paragraph, Should Be Withdrawn

The Office Action (8/27/02, page 3, #3) has rejected claims 1-20 under 35 U.S.C. §112, first paragraph, because the specification "does not reasonably provide enablement for a method that employs all fumonisin esterase or all amine oxidase encoding sequences and nucleotide sequences having at least 70% or 80% sequence identity to SEQ ID NO: 2, 4, 7, or 10 or hybridizing sequences thereof." This rejection is respectfully traversed. While the rejection has not been raised against newly submitted claims 21-33, the rejection will be addressed in so far as it may apply to the newly submitted claims.

In order to advance prosecution, claims 1, 10, and 18 (and thus claims 2-9 and newly added claims 21-22 and 29-33, which are dependent on or incorporate the limitations of claim 1; claims 11-17 and newly added claims 23-25, which are dependent on or incorporate the limitations of claim 10; and newly added claims 26-28, which are dependent on claim 18) have been amended to recite that the secondary nucleotide sequence has at least 90% identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10. These claims also include the limitation that the

secondary nucleotide sequence encodes a polypeptide having fumonisin detoxification activity. Claims 19 and 20 recite that at least one secondary nucleotide sequence is set forth in SEQ ID NO: 2, 4, 7, or 10.

As discussed in the specification, particularly for example on pages 9 and 11, the enzymes and nucleotide sequences of the present invention provide a means for continued catabolism of the fumonisin-degradation products obtained after degradation with other enzymes, such as, for example, the carboxylesterase and amine oxidase enzymes described in U.S. Patent Nos. 5,716,820, 6,025,188, and 6,229,071. The enzyme and nucleotide sequences of the present invention may also be used in combination with amino polyolamine oxidase enzymes, as also discussed, for example, on page 11. Thus, the primary nucleotide sequence of claim 1 may be a polypeptide having fumonisin esterase activity or a polypeptide having amine oxidase activity, and dependent claims 2 and 3 specify that the primary nucleotide sequence is ESP1 or BEST1, or an amino polyolamine oxidase (APAO), respectively. ESP1 and BEST1 are specific examples of fumonisin esterase enzymes, by which is meant any enzyme capable of hydrolysis of the ester linkage in fumonisin, as discussed on page 11 of the specification. The ESP1 and BEST1 sequences from the referenced patents have been incorporated into the substitute sequence listing submitted herewith; the ESP1 nucleotide sequence is set forth in SEQ ID NO:12 and the BEST1 nucleotide sequence is set forth in SEQ ID NO:14.

The present specification teaches assays for the claimed enzyme activities of the primary nucleotide sequence in addition to assays known in the art. Isolation and identification of esterase and amino polyolamine oxidase enzymes from an exemplary organism (*Exophiala spinifera)* are taught by the specification, particularly in working Example 1. Other additional methods are known in the art and taught in patents and applications incorporated by reference into the present specification, for example, U.S. Patent No. 5,716,820, which in Example 2 (column 19) teaches methods of cloning genes that encode fumonisin esterase. U.S. Patent No. 6,025,188, incorporated by reference, teaches in Example 13 a detailed assay for the demonstration of functional esterase activity. The primary nucleotide sequences may be isolated from other organisms, as illustrated by working examples in U.S. Pat. No. 6,211,434 of

sequences derived from *Rhinocladiella atrovirens* (SEQ ID NOs: 28-33 of the substitute sequence listing).

Similarly, the present specification teaches the limitations pertaining to the secondary nucleotide sequence by providing the exemplary nucleotide sequences of SEQ ID NOs: 2, 4, 7, and 10 and by teaching methods of sequence comparison on pages 17-20. The specification also teaches assays for fumonisin detoxification or degrading activity, as discussed in the specification for example on page 10 and illustrated in working Examples 3 and 4. In this manner, the specification teaches all the limitations of the primary and secondary nucleotide sequences of the claims.

Applicants have provided exemplary nucleotide sequences. The secondary nucleotide sequences of the claims vary from specified sequences by structural parameters (*i.e.*, percent sequence identity to SEQ ID NOs: 2, 4, 7, or 10). Guidance for determining percent identity of sequences is provided in the specification on pages 17 through 20. Applicants have also provided guidance for isolating and confirming a primary nucleotide sequence of the claims, and have provided assays for confirming the functional limitation of the secondary nucleotide sequence of the claims, *i.e.*, assays for fumonisin degradative or detoxification activity. Accordingly, one of skill in the art would be able to determine the functionality of polypeptides encompassed by the claimed invention. In newly-added claims 30-33, the primary nucleotide sequences also vary from specified sequences by structural parameters (*i.e.*, percent sequence identity to exemplary sequences).

Based on the guidance provided by the specification regarding the primary and secondary nucleotide sequences, the skilled artisan could choose among possible modifications to produce polypeptides within the parameters set forth in the claims and then test these modified variants to determine if they retain the desired activity. The Federal Circuit has repeatedly stated that enablement is not precluded by the necessity for some experimentation, so long as the experimentation needed to practice the invention is not undue. *In re Wands,* 8 USPQ2d 1400 (Fed. Cir. 1988). Furthermore, a considerable amount of experimentation is permissible, if it is

merely routine, or if the specification provides a reasonable amount of guidance by which the experimentation should proceed. *Id.*

Applicants stress that when evaluating the quantity of experimentation required, the court looks to the amount of experimentation required to practice a single embodiment of the invention, rather than the amount required to practice every embodiment of the invention. For example, in *Wands*, the claims at issue were drawn to immunoassay methods using any monoclonal antibody having a binding affinity for HbsAg of at least 10^{-9} M. The PTO had taken the position that the claim was not enabled as it would take undue experimentation to make the monoclonal antibodies required for the assay. The Federal Circuit reversed and held that the claims were enabled, as the amount of experimentation required to isolate monoclonal antibodies and screen for those having the correct affinity was not undue. *See Id.* Clearly, the Federal Circuit did not contemplate that every antibody useful in the methods of the claim must be identified. Rather, the court considered the amount of experimentation required to identify one or a few monoclonal antibodies having the required affinity. *See also, Johns Hopkins University v. Cellpro*, 931 F. Supp. 303, 324 (D. Del. 1996), *aff'd in part, vacated in part, and remanded*, 47 USPQ2d 1705 (Fed. Cir. 1998) (stating that the "specification need only enable one mode of making the claimed invention.").

In the instant case, the quantity of experimentation required to practice the invention amounts to three steps: stably integrating into a plant or plant cell a primary nucleotide sequence having fumonisin esterase activity or amine oxidase activity and stably integrating into a plant or plant cell a secondary nucleotide sequence that meets the sequence limitation of the claims and that has fumonisin detoxification activity. Such assays, while routine in the art, have further been presented in the specification on page 10 and in working Examples 1, 3, and 4.

Ample guidance is therefore provided to allow one of skill in the art to identify additional sequences encompassed by claims 1, 10, 18, 19, and 20 (and thus claims 2-9 and newly added claims 21-22 and 29-33, which are dependent on or incorporate the limitations of claim 1; claims 11-17 and newly added claims 23-25, which are dependent on or incorporate the limitations of claim 10; and newly added claims 26-28, which are dependent on claim 18). Consequently,

Applicants submit that the quantity of experimentation necessary and the amount of guidance presented in the specification is sufficient to enable the claimed plants, plant cells, and methods of use set forth in the claims. The rejection of the claims under 35 U.S.C. §112, first paragraph, for lack of enablement should be withdrawn and Applicants respectfully request that the rejection be not applied to the newly submitted claims.

The Office Action (8/27/02, page 6) has rejected claims 1-20 under 35 U.S.C. §112, first paragraph, "as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." This rejection is respectfully traversed. While the rejection has not been raised against newly submitted claims 21-33, the rejection will be addressed in so far as it may apply to the newly submitted claims. This rejection is addressed first with regard to the secondary nucleotide sequences of the claims and second with regard to the primary nucleotide sequences of the claims.

Claims 1, 10, and 18 (and thus claims 2-9 and newly added claims 21-22 and 29-33, which are dependent on or incorporate the limitations of claim 1; claims 11-17 and newly added claims 23-25, which are dependent on or incorporate the limitations of claim 10; and newly added claims 26-28, which are dependent on claim 18) have been amended to specify that the secondary nucleotide sequence has at least 90% identity to the exemplary sequence set forth in SEQ ID NO: 2, 4, 7, or 10. Support for these amendments can be found in the original claims and throughout the specification, more particularly, for example, on page 7.

Independent claims 1, 10, and 18 include the limitation that the secondary nucleotide sequence encodes a polypeptide having fumonisin detoxification activity. Claims 19 and 20 recite that at least one secondary nucleotide sequence is set forth in SEQ ID NO: 2, 4, 7, or 10. Newly added claims 21, 23, and 26 recite that the secondary nucleotide sequence has at least 95% sequence identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10, and newly added claims 22, 24, 25, and 28 recite that the secondary nucleotide sequence is the sequence set forth in SEQ ID NO: 2, 4, 7, or 10. Newly added claim 27 recites that the secondary nucleotide

sequence encodes the polypeptide set forth in SEQ ID NO: 3, 5, 8, or 11, and newly added claim 29 recites that the first and second promoter of the claims are the same promoter.

Applicants submit that the recitation of at least 90% sequence identity is a *very predictable structure* of the nucleotide sequences encompassed by the claimed invention. Applicants note that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2001). Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the secondary nucleotide sequences of the claimed invention, *i.e.*, a nucleotide sequence having at least 90% sequence identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10.

Furthermore, the description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See, Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), citing *Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs defined by nucleotide sequence and falling within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *See, Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, First Paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2001). The recitation of a predictable structure of at least 90% sequence identity to SEQ ID NO: 2, 4, 7, or 10 is sufficient to satisfy the written description requirement for the secondary nucleotide sequence of the claims.

Example 14 of the Revised Interim Written Description Guidelines is directed to a generic claim: a protein having at least 95% sequence identity to the sequence of SEQ ID NO: 3,

wherein the sequence catalyzes the reaction A → B. The Training Materials concludes that the generic claim of Example 14 is sufficiently described under § 112, first paragraph, because: 1) "the single sequence disclosed in SEQ ID NO: 3 is representative of the genus"; and 2) the claim recites a limitation requiring the compound to catalyze the reaction from A → B. The Guidelines conclude that one of skill in art would recognize that the Applicants were in possession of the necessary common attributes possessed by the members of the genus.

Following the analysis of Example 14, Applicants submit that the present claims satisfy the written description requirements of § 112, first paragraph. Specifically, the claims of the present invention encompass secondary nucleotide sequences having at least 90% sequence identity to SEQ ID NOs: 2, 4, 7, or 10 wherein the polypeptide has fumonisin degradative or detoxification activity. As in Example 14, the specification discloses the nucleic acid sequence of SEQ ID NOs: 2, 4, 7, and 10 and the claims recite a limitation requiring the compound to have a specific function (*i.e.*, fumonisin detoxification activity). Consequently, contrary to the Examiner's conclusion, the sequences encompassed by the claims are defined by relevant identifying physical and chemical properties. In fact, the common attributes or features of the elements possessed by the members of the secondary nucleotide sequence genus is that they encode polypeptides having fumonisin degradative or detoxification activity and share at least 90% sequence identity at the nucleotide level to the disclosed nucleotide sequences of SEQ ID NO: 2, 4, 7, or 10. The necessary common features of the claimed genus are clear. Accordingly, the written description requirement has been met.

With regard to the primary nucleotide sequences of the claims, amended independent claims 1, 10, and 18 continue to include the limitation that the primary nucleotide sequence encodes a polypeptide having fumonisin esterase activity or a polypeptide having amine oxidase activity. Applicants have provided exemplary sequences of the primary nucleotide sequences of the claims, for example, as incorporated by reference in the specification on pages 9 and 11 regarding ESP1, BEST1, and animo polyolamine oxidase enzymes and now included in the substitute sequence listing submitted herewith. Applicants submit that one of skill, using the

guidance of the specification, would be able to identify, isolate, and use a primary nucleotide sequence meeting the limitations of the claims, *i.e.*, a polypeptide having fumonisin esterase activity or amine oxidase activity, as exemplified by the referenced sequences. Guidance is provided in the specification, particularly on page 10 and in working Examples 3 and 4.

As discussed in the specification, particularly for example on pages 9 and 11, the enzymes and nucleotide sequences of the present invention provide a means for additional catabolism of the fumonisin-degradation products obtained from degradation with other enzymes, such as, for example, the carboxylesterase and amine oxidase enzymes previously described in U.S. Patent Nos. 5,716,820, 6,025,188, and 6,229,071. The enzyme and nucleotide sequences of the present invention may also be used in combination with amino polyolamine oxidase enzymes, as also discussed, for example, on page 11. Other amine oxidase enzymes are known in the art. See, for example, U.S. Pat. No. 5,792,931, issued August 11, 1998. Thus, the primary nucleotide sequence of claim 1 may be a polypeptide having fumonisin esterase activity or a polypeptide having amine oxidase activity, and dependent claims 2 and 3 specify that the primary nucleotide sequence is ESP1 or BEST1, or an amino polyolamine oxidase (APAO), respectively. ESP1 and BEST1 are specific examples of fumonisin esterase enzymes, by which is meant any enzyme capable of hydrolysis of the ester linkage in fumonisin, as discussed on page 11 of the specification.

The present specification teaches assays for the claimed enzyme activities of the primary nucleotide sequence in addition to assays known in the art. Isolation and identification of esterase and amino polyolamine oxidase enzymes from an exemplary organism (*Exophiala spinifera)* are taught by the specification, particularly in working Example 1. Other additional methods are known in the art and taught in the patents and applications incorporated by reference into the present specification. For example, U.S. Patent No. 5,716,820 teaches in Example 2 (column 19) methods of cloning genes that encode fumonisin esterase, and U.S. Patent No. 6,025,188 teaches in Example 13 a detailed assay for the demonstration of functional esterase activity.

While the above guidance is provided in the specification, Applicants emphasize that the primary nucleotide sequence may encode any enzyme having fumonisin esterase activity or amine oxidase activity. The presently claimed invention is drawn to the use of the novel secondary nucleotide sequences in conjunction with enzymes having fumonisin esterase activity or amine oxidase activity such as those previously described and cited in the specification. For these reasons, Applicants believe that this description of the primary nucleotide sequences meets the written description requirement.

Applicants note that newly added claims 30 and 32 specify that the primary nucleotide sequences have at least 80% sequence identity to specified exemplary sequences set forth in the sequence listing, and newly added claims 31 and 33 specify that the sequences share at least 90% sequence identity. As discussed above regarding such claim limitations, Applicants believe that the recitation of a high percentage of sequence identity is a very predictable structure of the primary nucleotide sequences encompassed by the claimed invention.

In summary, the description of a representative number of species *does not* require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Applicants submit that the relevant identifying physical and chemical properties of the disclosed genus would be clearly recognized by one of skill in the art and consequently, the Applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus. Accordingly, the rejection of claims 1-20 under 35 U.S.C. §112, first paragraph, for lack of written description should be withdrawn and not applied to the newly submitted claims.

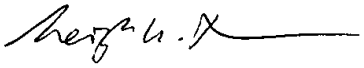
CONCLUSION

In view of the above amendments and remarks, Applicants submit that the rejections of the claims under 35 U.S.C. §§112, first and second paragraphs, are overcome. Applicants respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject Application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those, which may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



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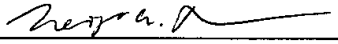

Leigh W. Thorne

Version with Markings to Show Changes Made:

In the Specification:

Please substitute the sequence listing filed concurrently herewith for the sequence listing filed on October 16, 2001.

Please revise the first full paragraph beginning on line 12, page 3, to read as follows:

Enzymes that degrade the fungal toxin fumonisin to the compound AP1 have been identified in U.S. Patent No. 5,716,820, U.S. Patent No. 6,025,188, and U.S. Patent No. 6,229,071, [and pending U.S. Patent Application Serial Nos. 08/888,949 and 08/888,950, both filed July 7, 1997, and] hereby incorporated by reference. Plants expressing a fumonisin esterase enzyme, infected by fumonisin producing fungus, and tested for fumonisin and AP1 were found to have low levels of fumonisin but high levels of AP1. AP1 is less toxic than fumonisin to plants and probably also animals, but contamination with AP1 is still a concern. The best result would be complete detoxification of fumonisin to a non-toxic form. Therefore enzymes capable of degrading AP1 are necessary for the further detoxification of fumonisin.

Please revise the first full paragraph beginning on line 12, page 8, to read as follows:

Thus, the genes and nucleotide sequences of the invention include both the naturally occurring sequences as well as mutant forms. Likewise, the proteins of the invention encompass both naturally occurring proteins as well as variations and modified forms thereof. Such variants will continue to possess the desired ability to degrade or catabolize fumonisin. Obviously, the mutations that will be made in the DNA encoding the variant must not place the sequence out of reading frame and preferably will not create complementary regions that could produce secondary mRNA structure. See, EP Patent [Application] Publication No. 75,444.

Please revise the first full paragraph beginning on line 11, page 9, to read as follows:

The carboxylesterase and amine oxidase have been previously described in U.S. Patent No. 5,716,820, U.S. Patent No. 6,025,188, and U.S. Patent No. 6,229,071 [and pending U.S.

Patent Application Serial Nos. 08/888,949 and 08/888,950]. Such disclosures are herein incorporated by reference. Thus, the sequences of the invention can be used in combination with those previously disclosed or disclosed in U.S. Patent No. 6,211,435 and U.S. Patent No. 6,211,434 [co-pending applications Serial Nos. 09/352,168 and 09/352,159], both entitled "Amino Polyolamine Oxidase Polynucleotides and Related Polypeptides and Methods of Use", herein incorporated by reference. These exemplary amino polyolamine oxidase nucleotide sequences are set forth in SEQ ID NOs: 16, 18, 20, 22, 24, 26, 28, 30, and 32. SEQ ID NO:16 is the same as SEQ ID NO:5 from U.S. Pat. No. 6,211,435; SEQ ID NO:18 is the same as SEQ ID NO:10 from U.S. Pat. No. 6,211,435; and SEQ ID NO:20 is the same as SEQ ID NO:22 from U.S. Pat. No. 6,211,435. The nucleotide sequences set forth in SEQ ID NOs: 16, 18, and 20 encode polypeptides having the amino acid sequences set forth in SEQ ID NOs: 17, 19, and 21, respectively (which are the same as SEQ ID NOs: 6, 11, and 23 from U.S. Pat. No. 6,211,435, respectively). Amino polyolamine oxidase nucleotide sequences of U.S. Pat. No. 6,211,434, with introns removed, are set forth in SEQ ID NOs:22 (SEQ ID NO:35 from U.S. Pat. No. 6,211,434), 24 (SEQ ID NO:37 from U.S. Pat. No. 6,211,434), 26 (SEQ ID NO:39 from U.S. Pat. No. 6, 211,434), 28 (SEQ ID NO:41 from U.S. Pat. No. 6,211,434), 30 (SEQ ID NO:43 from U.S. Pat. No. 6,211,434), and 32 (SEQ ID NO:45 from U.S. Pat. No. 6,211,434). The nucleotide sequences set forth in SEQ ID NOs: 22, 24, 26, 28, 30, and 32 encode polypeptides having the amino acid sequences set forth in SEQ ID NOs: 23, 25, 27, 29, 31, and 33, respectively (which are the same as SEQ ID NOs: 36, 38, 40, 42, 44, and 46 from U.S. Pat. No. 6,211,434, respectively). The enzymes and nucleotide sequences of the present invention provide a means for continued catabolism of the fumonisin-degradation products obtained after degradation with at least the carboxylesterase and amine oxidase.

Please revise the first full paragraph beginning on line 3, page 11, to read as follows:

By "fumonisin esterase" is meant any enzyme capable of hydrolysis of the ester linkage in fumonisin. Two examples of such enzymes are ESP1 and BEST1 found in U.S. Patent [Application] No. 5,716,820, U.S. Patent No. 6,025,188, and U.S. Patent No.6,229,071[pending

U.S. Application Serial Nos. 08/888,949 and 08/888,950, both filed July 7, 1997]. The ESP1 nucleotide sequence is set forth in SEQ ID NO:12 and is the same as SEQ ID NO:15 from U.S. Patent No. 6,025,188. This nucleotide sequence encodes a polypeptide having the amino acid sequence set forth in SEQ ID NO:13 (which is the same as SEQ ID NO:10 from U.S. Pat. No. 6,025,188). The BEST1 nucleotide sequence is set forth in SEQ ID NO:14 and is the same as SEQ ID NO:11 from U.S. Pat. No. 6,025,188. This nucleotide sequence encodes a polypeptide having the amino acid sequence set forth in SEQ ID NO: 15 (which is the same as SEQ ID NO:12 from U.S. Pat. No. 6,025,188).

Please revise the first full paragraph beginning on line 13, page 33, to read as follows:

Exophiala isolates from maize were isolated as described in U.S. Patent No. 5,716,820, U.S. Patent No. 6,025,188, and U.S. Patent No. 6,229,071, [and pending U.S. Application Serial Nos. 08/888,949 and 08/888,950, both filed July 7, 1997, and] herein incorporated by reference.

Please revise the first full paragraph beginning on line 15, page 34, to read as follows:

Agar cultures grown as above were used to inoculate YPD broth cultures (500 ml) in conical flasks at a final concentration of [105] 10^5 conidia per ml culture. Cultures were incubated 5 days at 28°C without agitation and mycelia harvested by filtration through 0.45 micron filters under vacuum. The filtrate was discarded, and the mycelial mat was washed and resuspended in sterile carbon-free, mineral salts medium (1 g/liter NH_3NO_4; 1 g/liter NaH_2PO_4; 0.5 g/liter $MgCl_2$; 0.1 g/liter NaCl; 0.13 g/liter $CaCl_2$; 0.02 g/liter $FeSO_4 \cdot 7H_20$, pH 4.5) containing 0.5 mg/ml alkaline hydrolyzed crude FB1. After 3-5 days at 28°C in the dark with no agitation the cultures were filtered through low protein binding 0.45 micron filters to recover the culture filtrate. Phenylmethyl sulfonyl fluoride (PMSF) was added to a concentration of 2.5 mM and the culture filtrate was concentrated using an Amicon™ YM10 membrane in a stirred cell at room temperature and resuspended in 50 mM sodium acetate, pH 5.2 containing 10 mM $CaCl_2$. The crude culture filtrate (approx. 200-fold concentrated) was stored at -20°C.

Please revise the first full paragraph beginning on line 26, page 37, to read as follows:

The polynucleotides were identified using a proprietary transcript imaging method that compares transcript patterns in two samples and allows cloning of differentially expressed fragments. This technology was developed by CuraGen® (New Haven, Connecticut) (see [Published] PCT Patent Application No. WO 97/15690, published May 1, 1997[,] and claiming priority from U.S. Application No. 08/663,823, which issued as U.S. Patent No. 5,972,693, all of which are [and] hereby incorporated by reference). Fluorescently-tagged, PCR amplified cDNA fragments representing expressed transcripts can be visualized as bands or peaks on a gel tracing, and the cDNA from differentially expressed (induced or suppressed) bands can be recovered from a duplicate gel, cloned, and sequenced. Known cDNAs can be identified without the need for cloning, by matching the predicted size and partially known sequence of specific bands on the tracing.

In the claims:

1. (Amended) A method of reducing pathogenicity of a fungus [producing] that produces fumonisin, comprising:

a) stably integrating into the genome of a plant cell a primary nucleotide sequence operably linked to a first promoter active in said plant cell, said primary nucleotide sequence comprising at least one sequence selected from the group consisting of a sequence encoding a polypeptide having fumonisin esterase activity and a sequence encoding a polypeptide having amine oxidase activity; and,

b) stably integrating into the genome of said plant cell a secondary nucleotide sequence operably linked to a second promoter active in said plant cell, wherein said secondary nucleotide sequence has at least 90% identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity. [comprises at least one sequence selected from the group consisting of:

a) a nucleotide sequence having at least 70% sequence identity to the nucleotide sequence set forth in SEQ ID NO: 2, 4, 7 or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity;

b) a nucleotide sequence having at least 80% sequence identity to the nucleotide sequence set forth in SEQ ID NO: 2, 4, 7 or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity;

c) a nucleotide sequence that hybridizes under stringent conditions to the complement of the nucleotide sequence set forth in SEQ ID NO: 2, 4, 7, or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity; and,

d) a nucleotide sequence encoded by the polypeptide set forth in SEQ ID NO: 3, 5, 8, or 11.]

3. (Amended) The method of claim 1, wherein said primary nucleotide sequence encoding a polypeptide having amine oxidase activity is [APAO] an amino polyolamine oxidase.

8. (Amended) The method of claim 1, [where said promoters are inducible] wherein at least one of said first promoter and said second promoter is an inducible promoter.

9. (Amended) The method of claim 8 further comprising inducing expression of said primary and said secondary nucleotide [sequence] sequences for a time sufficient to reduce pathogenicity of said fungus.

10. (Amended) A plant having stably integrating into its genome

a) a primary nucleotide sequence operably linked to a promoter active in said plant, said primary nucleotide sequence comprising at least one nucleotide sequence selected from the group consisting of a sequence encoding a polypeptide having fumonisin esterase activity or a sequence encoding a polypeptide having amine oxidase activity; and,

b) a secondary nucleotide sequence operably linked to a promoter active in said plant, wherein said secondary nucleotide sequence has at least 90% identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity. [comprises at least one sequence selected from the group consisting of:

i) a nucleotide sequence having at least 70% sequence identity to the nucleotide sequence set forth in SEQ ID NO: 2, 4, 7 or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity;

ii) a nucleotide sequence having at least 80% sequence identity to the nucleotide sequence set forth in SEQ ID NO: 2, 4, 7 or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity;

iii) a nucleotide sequence that hybridizes under stringent conditions to the complement of the nucleotide sequence set forth in SEQ ID NO: 2, 4, 7, or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity; and,

iv) a nucleotide sequence encoded by the polypeptide set forth in SEQ ID NO: 3, 5, 8, or 11.]

12. (Amended) The plant of claim 10, wherein said primary nucleotide sequence encoding a polypeptide having amine oxidase activity is [APAO] an amino polyolamine oxidase.

13. (Amended) The [method] plant of claim 10, wherein the primary nucleotide sequence stably incorporated into the plant cell comprises a sequence encoding a polypeptide having fumonisin esterase activity and a sequence encoding a polypeptide having amino oxidase activity.

17. (Amended) [The transformed] Transformed seed of the plant of claim 10.

18. (Amended) A plant cell having stably integrating into its genome

a) a primary nucleotide sequence operably linked to a promoter active in said plant cell, said primary nucleotide sequence comprising at least one nucleotide sequence selected from the group consisting of a sequence encoding a polypeptide having fumonisin esterase activity or a sequence encoding a polypeptide having amine oxidase activity; and,

b) a secondary nucleotide sequence operably linked to a promoter active in said plant, wherein said secondary nucleotide sequence has at least 90% identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity. [comprises at least one sequence selected from the group consisting of:

i) a nucleotide sequence having at least 70% sequence identity to the nucleotide sequence set forth in SEQ ID NO: 2, 4, 7 or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity;

ii) a nucleotide sequence having at least 80% sequence identity to the nucleotide sequence set forth in SEQ ID NO: 2, 4, 7 or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity;

iii) a nucleotide sequence that hybridizes under stringent conditions to the complement of the nucleotide sequence set forth in SEQ ID NO: 2, 4, 7, or 10, wherein said sequence encodes a polypeptide having fumonisin detoxification activity; and,

iv) a nucleotide sequence encoded by the polypeptide set forth in SEQ ID NO: 3, 5, 8, or 11.]

19. (Amended) A method of reducing pathogenicity of a fungus that produces [producing] fumonisin, comprising[:] stably integrating into the genome of a plant cell:

a) a primary nucleotide sequence operably linked to a promoter active in said plant cell, said primary nucleotide sequence comprising at least one nucleotide sequence selected from the group consisting of a sequence encoding a polypeptide having fumonisin esterase activity or a sequence encoding a polypeptide having amine oxidase activity; and,

b) a secondary nucleotide sequence operably linked to a promoter active in

said plant cell, wherein said secondary nucleotide sequence comprises at least one sequence selected from the group consisting of a nucleotide sequence set forth in one of SEQ ID NO: 2, 4, 7, and 10.

20. (Amended) A plant having stably integrating into its genome

a) a primary nucleotide sequence operably linked to a promoter active in said plant cell, said primary nucleotide sequence comprising at least one nucleotide sequence selected from the group consisting of a sequence encoding a polypeptide having fumonisin esterase activity or a sequence encoding a polypeptide having amine oxidase activity; and,

b) a secondary nucleotide sequence operably linked to a promoter active in said plant, wherein said secondary nucleotide sequence comprises at least one sequence selected from the group consisting of a nucleotide sequence set forth in one of SEQ ID NO: 2, 4, 7, and 10.